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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,198	03/26/2004	Didier Communi	9409/2113B	2940
29933	7590	04/12/2006	EXAMINER	
PALMER & DODGE, LLP			LI, RUIXIANG	
KATHLEEN M. WILLIAMS				
111 HUNTINGTON AVENUE			ART UNIT	PAPER NUMBER
BOSTON, MA 02199			1646	

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,198	COMMUNI ET AL.	
	Examiner Ruixiang Li	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 23 March 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 8-19 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-7 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 26 March 2004 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. 09/077,173.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>08/23/2004</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignment</u> . |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, Claims 1-7, in the reply filed on 03/23/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Applicants' preliminary amendment filed upon 08/24/2004 has been entered. Claims 1-19 are pending. Claims 1-7 are currently under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Information Disclosure Statement

3. The information disclosure statement filed on 08/23/2004 has been considered in full and a signed copy of the form PTO-1449 is attached to the office action.

Drawings

4. The drawings filed on 03/26/2004 are accepted by the Examiner.

Claim Rejections —35 U.S.C.§ 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-7 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-7 are drawn to an isolated antibody that specifically binds to a protein receptor comprising the amino acid sequence of SEQ ID NO: 2 and a pharmaceutical composition comprising the antibody. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not require further research.

The specification discloses that the polypeptide of SEQ ID NO: 2 belongs structurally to the purinergic receptor family (P2Y family) but functionally is a pyrimidinergic receptor, preferably a UTP-specific receptor (lines 25-27 of page 2). Nonetheless, the instant disclosure fails to provide any sufficient information or evidence on the specific biological functions or physiological significance of the molecules of the present invention and fails to disclose a patentable utility for the claimed invention.

The specification does not disclose a specific and substantial utility for the claimed invention. The specification discloses that incubation of the cells expressing the receptor protein of SEQ ID NO: 2 with UTP causes the accumulation of inositol triphosphate (see, e.g., Fig. 4). The specification asserts that the polypeptide of SEQ ID NO: 2 is a pyrimidinergic receptor, preferably a UTP-specific receptor (lines 25-27

of page 2) and an agonist or antagonist may be used in a pharmaceutical composition in the treatment of cystic fibrosis (lines 10-11 of page 7). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The disclosure neither identifies the biological functions of the polypeptide of SEQ ID NO: 2 nor establishes a causative link between the polypeptide of SEQ ID NO: 2 and cystic fibrosis. Clearly, further research would be required to identify the physiological roles of the molecules of the present invention or to establish a causative link between the polypeptide of SEQ ID NO: 2 and any particular disease, such as cystic fibrosis. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion".

The invention lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The sequence and prior art search does not reveal that the polypeptide of SEQ ID NO: 2 of the present invention or the antibody that binds to the polypeptide has a well-established utility. The specific physiological roles of the polypeptide of SEQ ID NO: 2 remain elusive even after the filing date of the instant application. As taught by Nicholas et al. (*Molecular Pharmacology* 50:224-229, 1996), "unambiguous evidence for regulated release of uridine nucleotides is needed to confirm the physiological importance of pyrimidinergic receptor-signaling responses (the third paragraph of

right column of page 228). Even the specific cellular activities of uridine nucleotides, the ligand of the receptor protein of SEQ ID NO: 2 of the present invention, remain unproved (top of left column of page 229).

No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the compounds.

7. Claims 1-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections—35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional

characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims 2-5 are drawn to an isolated antibody that specifically binds to a receptor comprising the amino acid sequence of SEQ ID NO: 2, wherein said antibody is *an agonist or antagonist of said receptor*, whereas claims 6 and 7 are drawn to a pharmaceutical composition comprising the antibody.

The specification discloses an isolated polypeptide of SEQ ID NO: 2 and an antibody that binds to the polypeptide. However, the instant disclosure does not adequately support the scope of the invention of claims 2-7 because the specification fails to provide a representative number of species of the claimed genus. In fact, the specification does not even disclose a single antibody that is an agonist or antagonist of the receptor protein of SEQ ID NO: 2. As acknowledged in the specification (line 11 of page 18), no specific antagonist was available for any P2Y subtype at the time of the filing of the instant application. It is noted that a description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure also fails to provide sufficient description information, such as definitive structural of the claimed antibody that would act as an agonist or antagonist of the receptor protein of SEQ ID NO: 2. Furthermore, the prior art does not provide

compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed antibodies as being identical to those instantly claimed.

Accordingly, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed antibodies that act as an agonist or antagonist of the receptor protein of SEQ ID NO: 2.

Conclusion

10. No Claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [Brenda.Brumback@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is

Art Unit: 1646

more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Ruixiang Li
Ruixiang Li, Ph.D.
Primary Examiner
April 9, 2006

RUIXIANG LI, PH.D.
PRIMARY EXAMINER

Scoring table:	BLOSUM62					
Gapop:	10.0 , Gapext: 0.5					
Searched:	2166443 seqs, 705528306 residues					
Total number of hits satisfying chosen parameters:	2166443					
Minimum DB seq length:	0					
Maximum DB seq length:	2000000000					
Post-processing:	Minimum Match 0% , Maximum Match 100%					
Database :	UniProt 05.80: 1: uniprot_sprot;* 2: uniprot_trembl;*					
Pred. No.	is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.					
SUMMARIES						
Result No.	Query	Match	Length	DB	ID	Description
1	1944	100.0	365	1	P2RY4_HUMAN	P51582 homo sapien
2	1944	100.0	365	2	Q5J25_HUMAN	Q5J22 homo sapien
3	1938	99.7	365	2	Q502W_HUMAN	Q50W2 homo sapien
4	1935	99.5	365	2	QAVBB7_HUMAN	Q4vb7 homo sapien
5	1934	99.5	365	2	Q4VBB8_HUMAN	Q4vb8 homo sapien
6	1597	82.2	361	1	P2RY4_RAT	Q35H11 rattus norvegicus
7	1561	80.3	361	1	P2RY4_MOUSE	Q91jj7 mus musculus
8	1176	60.5	230	2	QSY805_PIG	Q5Y09 sus scrofa
9	1127	58.5	374	2	Q5T466_MENGA	Q5T466 meleagris gallopavo
10	1038	53.4	347	2	Q7Z2A4_BRARE	Q7224 brachydanio rerio
11	1022	52.6	543	2	Q5B179_XENTR	Q5b179 xenopus laevis
12	1007	51.5	537	1	P2RY8_XENLA	P75928 xenopus laevis
13	1007	51.5	537	2	Q7ZHQ7_XENLA	Q7zwq7 xenopus laevis
14	970	55.5	302	1	Q4RP73_TETING	Q4rp73 tetradon nigroviridis
15	965	49.6	377	1	P2RY2_HUMAN	P41231 homo sapien
16	962	49.5	373	1	P2RY2_MOUSE	P33383 mus musculus
17	950	48.9	374	1	P2RY2 RAT	P41232 rattus norvegicus
18	940	48.4	373	2	Q5Y2A5_PIG	Q5yra5 sus scrofa
19	910	46.8	349	2	Q6PB52_XENTR	Q5pb52 xenopus laevis
20	823	42.3	165	1	P2RY4_CTRCTR	P5826 cricetus citellus
21	809	41.6	164	1	Q5DCK1_PIG	Q5dk1 sus scrofa
22	803	41.3	310	2	Q4SEL5_TEING	Q4sel5 tetrodon nigroviridis
23	611	34.1	125	1	Q6QH9_BOVIN	Q6qh9 bos taurus
24	611	33.0	373	1	P2RY1_HUMAN	P47900 homo sapien
25	631	32.5	362	1	P2RY1_MELGA	P49652 meleagris gallopavo
26	628	32.3	362	1	P2RY3_CHICK	P4996 gallus gallus
27	628	32.3	373	1	P2RY1_CAVEO	P59902 carica papaya
28	621	31.9	373	1	P2RY1_BOVIN	P48042 bos taurus
29	620	31.9	357	2	Q9DE05_RAIDER	Q9de05 raja erinaceus
30	616	31.7	373	1	P2RY1 RAT	P49651 rattus norvegicus
31	614	31.6	373	1	P2RY1_MOUSE	P49650 mus musculus

agonist-dependent desensitization and loss of surface P2RY4; This phosphorylation does not involve PKC, nor other calcium activated kinases.

-1- SIMILARITY: Belongs to the G-protein coupled receptor 1 family.

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EMBL; X91852; CBA62263.1; -; Genomic DNA.
 EMBL; U40223; AAC50347.1; -; Genomic DNA.
 EMBL; X96597; CRA65415.1; -; Genomic DNA.
 DR HSSP; P34996; 1DDD.
 DR Ensemble; ENSG00000186912; Homo sapiens.
 DR HGNC; HGNC-8542; P2RY4.
 DR MIM; 300038; -.
 DR GO; GO:0005887; C:integral to plasma membrane; TAS.
 DR GO; GO:0007204; P:positive regulation of cytosolic calcium io. . . ; TAS.
 DR InterPro; IPR00276; GPCR_RhoGDP.
 DR InterPro; IPR002286; P2_purinceptor.
 DR InterPro; IPR000018; P2Y4_purinceptor.
 DR Pfam; PF00001; 7tm_1; 1.
 DR PRINTS; PRO0237; GPCR_RHODOPSN.
 DR PRINTS; PRO1066; P2Y4_PRRNODPPTR.
 DR PROSITE; PS00231; G_PROTEIN_RECEP_F1_1; 1.
 DR PROSITE; PS50265; G_PROTEIN_RECEP_F1_2; 1.
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 FT TOPO_DOM 1 34 Extracellular (Potential).
 FT TRANSEM 35 61 1 (Potential).
 FT TOPO_DOM 62 72 Cytoplasmic (Potential).
 FT TRANSEM 73 95 2 (Potential).
 FT TOPO_DOM 96 112 Extracellular (Potential).
 FT TRANSEM 113 131 3 (Potential).
 FT TOPO_DOM 132 154 Cytoplasmic (Potential).
 FT TRANSEM 155 174 4 (Potential).
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 FT TRANSEM 197 222 5 (Potential).
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 FT MOD_RS5 333 333 Phosphosine (Probable).
 FT MOD_RS5 334 334 Phosphoserine (Probable).
 FT DISTI_PTD 108 185 By similarity.
 FT VARIANT 168 168 V -> M (in dbSNP 1152186).
 FT /FTId=VAR_011854 /FTId=VAR_011855
 FT VARIANT 178 178 N -> T (in dbSNP 1152187).
 FT /FTId=VAR_011855
 FT VARIANT 191 191 P -> L (in dbSNP 1152188).
 FT /FTId=VAR_011856.
 FT MUTAGEN 243 243 S->A: No effect.
 FT MUTAGEN 333 365 Missing: Abolishes agonist-induced phosphorylation. Prevents agonist-induced desensitization and loss of cell surface receptors.

SSNALVSQPEDSSCRWATPODSSCSPT->AAIALVALPEDA ACTWAAPODAACAA: Greatly reduces agonist-induced desensitization and loss of cell surface receptors.

S->A: Greatly reduces agonist-induced desensitization and loss of cell surface receptors; when associated with A-334 and A-339.

S->A: Greatly reduces agonist-induced desensitization and loss of cell surface receptors; when associated with A-333 and A-334.

Missing: No effect on agonist-induced phosphorylation, no functional effect.

Missing: No functional effect.

L -> V (in Ref. 2).

S -> A (in Ref. 2).

FT MUTAGEN 333 359
 FT MUTAGEN 333 333
 FT MUTAGEN 334 334

A-319. Greatly reduces agonist-induced desensitization and loss of cell surface receptors; when associated with A-333 and A-334.

Missing: No effect on agonist-induced phosphorylation, no functional effect.

Missing: No functional effect.

Score 1944; DB 1; Length 365;
 Pred. No. 1..e-131; Mismatches 0; Gaps 0;

Query Match Score 100.0%; Best Local Similarity 100.0%; Matches 365; Conservative 0; Mismatches 0; Gaps 0;

Qy 1 MASTESSLRLSLIGLSPGPSSSEVLDCWFDDEDFFKPLIPSYAVTFVGLNAPTLMLP 60
 Db 1 MASTESSLRLSLIGLSPGPSSSEVLDCWFDDEDFFKPLIPSYAVTFVGLNAPTLMLP 60

Qy 61 IFRLRPWDATATMFLALSDTLYNLISLPLTLYYYAARNHWPFETICKFVRFIFYNNLY 120
 Db 61 IFRLRPWDATATMFLALSDTLYNLISLPLTLYYYAARNHWPFETICKFVRFIFYNNLY 120

Qy 121 CSVFLTC1SVRHLIGCHICPLRAILWRGRPLAGLCLAWLVVGLCPNLLPFVTTNSKG 180
 Db 121 CSVFLTC1SVRHLIGCHICPLRAILWRGRPLAGLCLAWLVVGLCPNLLPFVTTNSKG 180

Qy 181 TTVLCHDTRPEEFDHVFHESVAVMGLLFGVPC1LYTLCYGLMARRLYQPLPGSAQSSR 240
 Db 181 TTVLCHDTRPEEFDHVFHESVAVMGLLFGVPC1LYTLCYGLMARRLYQPLPGSAQSSR 240

Qy 241 LRSARTIAVLLTVAVCFYPHTITTYLARLEADCRVNINIVVYKTRPLASANSC 300
 Db 241 LRSARTIAVLLTVAVCFYPHTITTYLARLEADCRVNINIVVYKTRPLASANSC 300

Qy 301 LDPPVYLTSQDKYRQLROLCGGKGPQRTAASSLALVSPLPEDDSSCRWATPODSSCSTP 360
 Db 301 LDPPVYLTSQDKYRQLROLCGGKGPQRTAASSLALVSPLPEDDSSCRWATPODSSCSTP 360

Qy 361 RADRL 365
 Db 361 RADRL 365

RESULT 2
 ID Q5JTP2_HUMAN PRELIMINARY; PRT; 365 AA.
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 DT 10-MAY-2005 (TREMBUREL 30, Last sequence update)
 DT 13-SEP-2005 (TREMBUREL 31, Last annotation update)
 DB Pyrimidinergic receptor_P2Y, G-protein coupled, 4 (Pyrimidinergic receptor_P2Y4).
 GN Name=P2RY4; ORFNames=RP13-26D14.5-001;
 OS Homo sapiens (Human).
 OC Bokaryota; Metazoa; Chordata; Craniata; Vertebrata; Ruteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
 OC Homo.
 RN [1] NUCLEOTIDE SEQUENCE
 RA Brown A.; Submitted (MAY-2005) to the EMBL/GenBank/DDBJ databases.
 RL [2]
 RN NUCLEOTIDE SEQUENCE.
 RP PCR rescued clones.
 RC MEDLINE=2238257; PubMed=124797932; DOI=10.1073/pnas.242603899;
 RX Strausberg R.L., Feingold B.A., Grouse L.H., Derge J.G.,
 RA Klauser R.D., Colling F.S., Wagner L., Shevchenko A.M., Schuler G.D.,
 RA Altshuller S.P., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Datchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,